PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference	**FOR FURTHER ACTION**	see Form PCT/ISA/220 as well as, where applicable, item 5 below.
30528WO-1ORD		
International application No.	International filing date *(day/month/year)*	(Earliest) Priority Date *(day/month/year)*
PCT/US2009/045635	29/05/2009	30/05/2008
Applicant		
SAMPATH, Rangarajan		

This international search report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This international search report consists of a total of 9 sheets.

☐ It is also accompanied by a copy of each prior art document cited in this report.

1. **Basis of the report**
   a. With regard to the **language,** the international search was carried out on the basis of:
      ☒ the international application in the language in which it was filed
      ☐ a translation of the international application into _____, which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1(b))
   b. ☐ This international search report has been established taking into account the **rectification of an obvious mistake** authorized by or notified to this Authority under Rule 91 (Rule 43.6*bis*(a)).
   c. ☒ With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, see Box No. I.

2. ☒ **Certain claims were found unsearchable** (See Box No. II)

3. ☒ **Unity of invention is lacking** (see Box No III)

4. With regard to the **title,**
   ☒ the text is approved as submitted by the applicant
   ☐ the text has been established by this Authority to read as follows:

5. With regard to the **abstract,**
   ☒ the text is approved as submitted by the applicant
   ☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box No. IV. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority

6. With regard to the **drawings,**
   a. the figure of the **drawings** to be published with the abstract is Figure No. _____
      ☐ as suggested by the applicant
      ☐ as selected by this Authority, because the applicant failed to suggest a figure
      ☐ as selected by this Authority, because this figure better characterizes the invention
   b. ☒ none of the figures is to be published with the abstract

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2009/045635

Box No. I Nucleotide and/or amino acid sequence(s) (Continuation of item 1.b of the first sheet)

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, the international search was carried out on the basis of:

   a. type of material

   [X] a sequence listing

   [ ] table(s) related to the sequence listing

   b. format of material

   [X] on paper

   [X] in electronic form

   c. time of filing/furnishing

   [X] contained in the international application as filed

   [X] filed together with the international application in electronic form

   [ ] furnished subsequently to this Authority for the purpose of search

2. [ ] In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

3. Additional comments:

A. CLASSIFICATION OF SUBJECT MATTER
INV. C12Q1/68

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
C12Q

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, EMBASE, BIOSIS, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	FARLOW J ET AL: "Francisella tularensis strain typing using multiple-locus variable-number tandem repeat analysis" JOURNAL OF CLINICAL MICROBIOLOGY, WASHINGTON, DC, US, vol. 39, no. 9, 1 September 2001 (2001-09-01), pages 3186-3192, XP002963868 ISSN: 0095-1137 the whole document	1-46

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[X] Further documents are listed in the continuation of Box C.

[X] See patent family annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
27 July 2009	07/10/2009

Name and mailing address of the ISA/	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Franz, Cerstin

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C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	JOHANSSON A ET AL: "Evaluation of PCR-based methods for discrimination of Francisella species and subspecies and development of a specific PCR that distinguishes the two major subspecies of Francisella tularensis." JOURNAL OF CLINICAL MICROBIOLOGY NOV 2000, vol. 38, no. 11, November 2000 (2000-11), pages 4180-4185, XP002538882 ISSN: 0095-1137 the whole document	1-46
Y	BARNS SUSAN M ET AL: "Detection of diverse new Francisella-like bacteria in environmental samples." APPLIED AND ENVIRONMENTAL MICROBIOLOGY SEP 2005, vol. 71, no. 9, September 2005 (2005-09), pages 5494-5500, XP002538883 ISSN: 0099-2240 the whole document	1-46
Y	DE LA PUENTE-REDONDO V A ET AL: "Comparison of different PCR approaches for typing of Francisella tularensis strains." JOURNAL OF CLINICAL MICROBIOLOGY MAR 2000, vol. 38, no. 3, March 2000 (2000-03), pages 1016-1022, XP002538884 ISSN: 0095-1137 the whole document	1-46
X	ECKER DAVID J ET AL: "Rapid identification and strain-typing of respiratory pathogens for epidemic surveillance." PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA 31 MAY 2005, vol. 102, no. 22, 31 May 2005 (2005-05-31), pages 8012-8017, XP002538885 ISSN: 0027-8424 the whole document	47-52

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C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	GARCÍA DEL BLANCO N ET AL: "Genotyping of Francisella tularensis strains by pulsed-field gel electrophoresis, amplified fragment length polymorphism fingerprinting, and 16S rRNA gene sequencing." JOURNAL OF CLINICAL MICROBIOLOGY AUG 2002, vol. 40, no. 8, August 2002 (2002-08), pages 2964-2972, XP002538886 ISSN: 0095-1137 the whole document	1-52
A	WO 03/102191 A (SECR DEFENCE [GB]; PRIOR JOANN LISA [GB]; PRIOR RICHARD GEOFFREY [GB];) 11 December 2003 (2003-12-11) the whole document	1-52
A	WO 2004/013357 A (UNIV CALIFORNIA [US]) 12 February 2004 (2004-02-12) the whole document	1-52

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box II.2

Claims Nos.: -

Present claims 1-52 relate to an unlimited number of possible nucleic acid primer sequences and their use in methods for amplification and detection of Francisella. The possible nucleic acid sequence compositions claimed lead to an unlimited number of arbitrary primer pairs that are neither sufficiently disclosed nor supported as primers for amplification of Francisella, contrary to the requirements of Article 5 and 6 PCT. In fact, the claims contain so many options that a lack of clarity withing the meaning of Article 6 arises to such an extend as to render a meaningful search of the claims impossible.

It has to be pointed out with regard to the unity reasoning below (see item IV) that the validity of each primer nucleic acid sequence composition has to be sufficiently disclosed and supported according to the requirements of Article 5 and 6 PCT. This will have to be considered in particular when paying for further inventions.

Consequently, a search could be carried out for those parts of the application which appear to be clear and which are sufficiently disclosed and supported, namely:

Primer pairs as defined by SEQ ID NOS#: 1:3, 2:4, 5:40, 6:41, 7:42, 8:43, 9:44, 10:45, 11:46, 12:47, 13:48, 14:49, 15:50, 16:51, 17:52, 18:53, 19:54, 20:55, 21:56, 22:57, 23:58, 24:59, 25:60, 26:61, 27:62, 28:63, 29:64, 30:65, 31:66, 32:67, 33:68, 34:69, 35:70, 36:71, 37:72, 38:73, 39:74, 75:76, 77:78, 79:80 and 81:82 (as defined in table 1 of the description and claim 4) and their us in methods for detection of Francisella.

The applicant's attention is drawn to the fact that claims relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure. If the application proceeds into the regional phase before the EPO, the applicant is reminded that a search may be carried out during examination before the EPO (see EPO Guideline C-VI, 8.2), should the problems which led to the Article 17(2)PCT declaration be overcome.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2009/045635

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☒ Claims Nos.: -
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

see FURTHER INFORMATION sheet PCT/ISA/210

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers allsearchable claims.

2. ☐ As all searchable claims could be searched without effort justifying an additional fees, this Authority did not invite payment of additional fees.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search reportcovers only those claims for which fees were paid, specifically claims Nos.:

4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

1 - 52 (all partially)

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.

☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.

☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

Invention 1: claims 1-52 (all partially)

A composition comprising the purified oligonucleotide primer pair consisting of SEQ ID NOS# 1:3; a kit comprising said primer pair; a method of determining a presence of a Francisella in at least one sample by amplification; a method of identifying one or more Francisella bioagents in a sample by amplification and determining molecular masses or base compositions of amplified products and a system comprising a mass spectrometer to detect molecular masses of amplicons and a system comprising a mass spectrometer for detection of molecular masses of amplicons.

Invention 2: claims 1-52 (all partially)

A composition comprising the purified oligonucleotide primer pair consisting of SEQ ID NOS# 2:4; a kit comprising said primer pair; a method of determining a presence of a Francisella in at least one sample by amplification; a method of identifying one or more Francisella bioagents in a sample by amplification and determining molecular masses or base compositions of amplified products and a system comprising a mass spectrometer to detect molecular masses of amplicons and a system comprising a mass spectrometer for detection of molecular masses of amplicons.

Inventions 3-42: claims 1-52 (all partially)

A composition comprising the purified oligonucleotide primer pair consisting of SEQ ID NOS# 5:40, 6:41, 7:42, 8:43, 9:44, 10:45, 11:46, 12:47, 13:48, 14:49, 15:50, 16:51, 17:52, 18:53, 19:54, 20:55, 21:56, 22:57, 23:58, 24:59, 25:60, 26:61, 27:62, 28:63, 29:64, 30:65, 31:66, 32:67, 33:68, 34:69, 35:70, 36:71, 37:72, 38:73, 39:74, 75:76, 77:78, 79:80 and 81:82, respectively; a kit comprising said primer pair; a method of determining a presence of a Francisella in at least one sample by amplification; a method of identifying one or more Francisella bioagents in a sample by amplification and determining molecular masses or base compositions of amplified products and a system comprising a mass spectrometer to detect molecular masses of amplicons and a system comprising a mass spectrometer for detection of molecular masses of amplicons.

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 03102191 A	11-12-2003	AU 2003234043 A1	19-12-2003
		CA 2487724 A1	11-12-2003
		CN 1671845 A	21-09-2005
		EP 1509607 A1	02-03-2005
		JP 2005528108 T	22-09-2005
		US 2007128225 A1	07-06-2007
WO 2004013357 A	12-02-2004	AU 2003269938 A1	23-02-2004
		US 2006040268 A1	23-02-2006
		US 2007111248 A1	17-05-2007

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

see form PCT/ISA/220

PCT

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43*bis*.1)

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION
See paragraph 2 below

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/US2009/045635	29.05.2009	30.05.2008

International Patent Classification (IPC) or both national classification and IPC
INV. C12Q1/68

Applicant
SAMPATH, Rangarajan

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☒ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☒ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☒ Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notifed the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:	Date of completion of this opinion	Authorized Officer
European Patent Office P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk - Pays Bas Tel. +31 70 340 - 2040 Fax: +31 70 340 - 3016	see form PCT/ISA/210	Franz, Cerstin Telephone No. +31 70 340-9463

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of:

   ☒ the international application in the language in which it was filed

   ☐ a translation of the international application into , which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1 (b)).

2. ☐ This opinion has been established taking into account the **rectification of an obvious mistake** authorized by or notified to this Authority under Rule 91 (Rule 43bis.1(a))

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

   a. type of material:

   ☒ a sequence listing

   ☐ table(s) related to the sequence listing

   b. format of material:

   ☒ on paper

   ☒ in electronic form

   c. time of filing/furnishing:

   ☒ contained in the international application as filed.

   ☒ filed together with the international application in electronic form.

   ☐ furnished subsequently to this Authority for the purposes of search.

4. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

5. Additional comments:

Box No. II Priority

1. ☒ The validity of the priority claim has not been considered because the International Searching Authority does not have in its possession a copy of the earlier application whose priority has been claimed or, where required, a translation of that earlier application. This opinion has nevertheless been established on the assumption that the relevant date (Rules 43*bis*.1 and 64.1) is the claimed priority date.

2. ☐ This opinion has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid (Rules 43*bis*.1 and 64.1). Thus for the purposes of this opinion, the international filing date indicated above is considered to be the relevant date.

3. Additional observations, if necessary:

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of

☐ the entire international application

☒ claims Nos. 1-52 all partially

because:

☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international search *(specify)*:

☒ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. 1-52 are so unclear that no meaningful opinion could be formed *(specify)*:

see separate sheet

☒ the claims, or said claims Nos. 1-52 are so inadequately supported by the description that no meaningful opinion could be formed *(specify)*:

see separate sheet

☒ no international search report has been established for the whole application or for said claims Nos. 1-52

☐ a meaningful opinion could not be formed without the sequence listing; the applicant did not, within the prescribed time limit:

- ☐ furnish a sequence listing on paper complying with the standard provided for in Annex C of the Administrative Instructions, and such listing was not available to the International Searching Authority in a form and manner acceptable to it.
- ☐ furnish a sequence listing in electronic form complying with the standard provided for in Annex C of the Administrative Instructions, and such listing was not available to the International Searching Authority in a form and manner acceptable to it.
- ☐ pay the required late furnishing fee for the furnishing of a sequence listing in response to an invitation under Rules 13*ter*.1(a) or (b).

☐ a meaningful opinion could not be formed without the tables related to the sequence listings; the applicant did not, within the prescribed time limit, furnish such tables in electronic form complying with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions, and such tables were not available to the International Searching Authority in a form and manner acceptable to it.

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in electronic form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ See Supplemental Box for further details

Box No. IV Lack of unity of invention

1. ☒ In response to the invitation (Form PCT/ISA/206) to pay additional fees, the applicant has, within the applicable time limit:

   ☐ paid additional fees

   ☐ paid additional fees under protest and, where applicable, the protest fee

   ☐ paid additional fees under protest but the applicable protest fee was not paid

   ☒ not paid additional fees

2. ☐ This Authority found that the requirement of unity of invention is not complied with and chose not to invite the applicant to pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rule 13.1, 13.2 and 13.3 is

   ☐ complied with

   ☒ not complied with for the following reasons:

   see separate sheet

4. Consequently, this report has been established in respect of the following parts of the international application:

   ☐ all parts.

   ☒ the parts relating to claims Nos. 1-52 (all partially)

Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-46
	No:	Claims	47-52
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-52
Industrial applicability (IA)	Yes:	Claims	1-52
	No:	Claims	

2. Citations and explanations

see separate sheet

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

Reference is made to the following documents:

D1: FARLOW J ET AL: "Francisella tularensis strain typing using multiple-locus variable-number tandem repeat analysis" JOURNAL OF CLINICAL MICROBIOLOGY, WASHINGTON, DC, US, vol. 39, no. 9, 1 September 2001 (2001-09-01), pages 3186-3192, XP002963868 ISSN: 0095-1137

D2: JOHANSSON A ET AL: "Evaluation of PCR-based methods for discrimination of Francisella species and subspecies and development of a specific PCR that distinguishes the two major subspecies of Francisella tularensis." JOURNAL OF CLINICAL MICROBIOLOGY NOV 2000, vol. 38, no. 11, November 2000 (2000-11), pages 4180-4185, XP002538882 ISSN: 0095-1137

D3: BARNS SUSAN M ET AL: "Detection of diverse new Francisella-like bacteria in environmental samples." APPLIED AND ENVIRONMENTAL MICROBIOLOGY SEP 2005, vol. 71, no. 9, September 2005 (2005-09), pages 5494-5500, XP002538883 ISSN: 0099-2240

D4: DE LA PUENTE-REDONDO V A ET AL: "Comparison of different PCR approaches for typing of Francisella tularensis strains." JOURNAL OF CLINICAL MICROBIOLOGY MAR 2000, vol. 38, no. 3, March 2000 (2000-03), pages 1016-1022, XP002538884 ISSN: 0095-1137

Item III:

Present claims 1-52 relate to an unlimited number of possible nucleic acid primer sequences and their use in methods for amplification and detection of Francisella. The possible nucleic acid sequence compositions claimed lead to an unlimited number of arbitrary primer pairs that are neither sufficiently disclosed nor supported as primers for amplification of Francisella, contrary to the requirements of Article 5 and 6 PCT. In fact, the claims contain so many options that a lack of clarity withing the meaning of Article 6 arises to such an extend as to render a meaningful search of the claims impossible.

It has to be pointed out with regard to the unity reasoning below (see item IV) that the validity of each primer nucleic acid sequence composition has to be sufficiently disclosed

and supported according to the requirements of Article 5 and 6 PCT. This will have to be considered in particular when paying for further inventions.

Consequently, a search could be carried out for those parts of the application which appear to be clear and which are sufficiently disclosed and supported, namely:

Primer pairs as defined by SEQ ID NOS#: 1:3, 2:4, 5:40, 6:41, 7:42, 8:43, 9:44, 10:45, 11:46, 12:47, 13:48, 14:49, 15:50, 16:51, 17:52, 18:53, 19:54, 20:55, 21:56, 22:57, 23:58, 24:59, 25:60, 26:61, 27:62, 28:63, 29:64, 30:65, 31:66, 32:67, 33:68, 34:69, 35:70, 36:71, 37:72, 38:73, 39:74, 75:76, 77:78, 79:80 and 81:82 (as defined in table 1 of the description and claim 4) and their us in methods for detection of Francisella.

Item IV:

With regard to the complexity reasoning as provided above, the common concept of the application as defined by the appended claims is the provision of products comprising primer pairs and methods using such for detection of Francisella. However, this concept is not novel in view of D1 disclosing primer pairs for strain typing of Francisella employing multiple-locus variable-number tandem repeat (VNTR) analysis (whole document).
The common concept is further not novel in view of e.g. D2-D4 (whole documents) all disclosing pairs of primers for identification/detection of Francisella. The primer pairs claimed in the present invention do not share any further common structural or functional feature. Consequently, in view of this prior art primer pairs used for amplification and detection of Francisella are known and cannot be seen as a special technical feature in the sense of Rule 13(2) PCT. The problem to be solved is thus to be considered as the provision of further primer pairs for amplification and detection of Francisella. The solutions provided by the present application as defined by the present claims (with regard to the complexity reasoning provided under item III) are the 42 primer pairs as identified in claim 4 and table 1 of the description. Each primer pair represents an alternative solution to the problem posed and gives rise to the following inventions:

Invention 1:

A composition comprising the purified oligonucleotide primer pair consisting of SEQ ID NOS# 1:3; a kit comprising said primer pair; a method of determining a presence of a Francisella in at least one sample by amplification; a method of identifying one or more Francisella bioagents in a sample by amplification and determining molecular masses or base compositions of amplified products and a system comprising a mass spectrometer to detect molecular masses of amplicons and a system comprising a mass spectrometer for detection of molecular masses of amplicons (claims 1-52 all partially).

Invention 2:

A composition comprising the purified oligonucleotide primer pair consisting of SEQ ID NOS# 2:4; a kit comprising said primer pair; a method of determining a presence of a Francisella in at least one sample by amplification; a method of identifying one or more Francisella bioagents in a sample by amplification and determining molecular masses or base compositions of amplified products and a system comprising a mass spectrometer to detect molecular masses of amplicons and a system comprising a mass spectrometer for detection of molecular masses of amplicons (claims 1-52 all partially).

Inventions 3-42:

A composition comprising the purified oligonucleotide primer pair consisting of SEQ ID NOS# 5:40, 6:41, 7:42, 8:43, 9:44, 10:45, 11:46, 12:47, 13:48, 14:49, 15:50, 16:51, 17:52, 18:53, 19:54, 20:55, 21:56, 22:57, 23:58, 24:59, 25:60, 26:61, 27:62, 28:63, 29:64, 30:65, 31:66, 32:67, 33:68, 34:69, 35:70, 36:71, 37:72, 38:73, 39:74, 75:76, 77:78, 79:80 and 81:82, respectively; a kit comprising said primer pair; a method of determining a presence of a Francisella in at least one sample by amplification; a method of identifying one or more Francisella bioagents in a sample by amplification and determining molecular masses or base compositions of amplified products and a system comprising a mass spectrometer to detect molecular masses of amplicons and a system comprising a mass spectrometer for detection of molecular masses of amplicons (claims 1-52 all partially).

Because no other technical features can be distinguished which, in view of the prior art could be regarded as special technical features in the sense of Rule 13(2) PCT, the ISA is

of the opinion that there is not single inventive concept underlying the plurality of claimed inventions of the present application in the sense of Rule 13(1) PCT.

The applicant is reminded that claims or parts thereof for which no International Search Report has been established, will not be the subject of the International Preliminary Examination (Rules 66.1e; 70.2d PCT). This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

What follows is an opinion on the patentability of invention 1 (claims 1-52 all partially) as defined above.

Item V:

Novelty (Article 33(2) PCT)

A primer pair consisting of the oligonucleotides as defined by SEQ ID NOS# 1 and 3 are novel with regard to the prior art identified.

Consequently, are methods employing such primers for amplification also novel.

Claims 1-46 are novelty and thus comply with the requirements of Article 33(2) PCT.
D5 discloses a system according to claim 47 comprising a mass spectrometer and a controller that is suitable for identification and strain-typing of viral and bacterial pathogens by electrospray ionization mass spectrometry. This system is also suitable for detection of Francisella when using appropriate primers (see objections raised under item VIII).

Thus, claims 47-52 are not novel and thereby don't comply with the requirements of Article 33(2) PCT.

Inventive Step (Article 33(3) PCT)

The primer pair consisting of oligonucleotides as defined by SEQ ID NOS# 1 and 3

constitute merely an alternative primer pair for identification or characterization or strain typing etc. of Francisella. The prior art provides multiple such primer pairs employed in respective applications (D1-D4). The design of such primer pairs and their use for amplification/detection/strain-typing of Francisella is therefore considered a routine procedure for the skilled person that he would be able to carry out with regard to the prior art identified. The primer pair as defined by SEQ ID NOS# 1 and 3 does not provide an unexpected, surprising effect or technical advantage over the routine procedures known and described in the field of Francisella amplification and detection.

Thus, the primer pair as defined by SEQ ID NOS# 1 and 3 is not inventive.

Consequently, compositions and kits comprising such and known routine methods using said primers are not inventive either.

Claims 1-52 are not inventive and thus do not comply with the requirements of Article 33(3) PCT.

Industrial applicability (Article 33(4) EPC)

Claims 1-52 appear industrially applicable in the sense of Article 33(4) PCT.

Item VIII:

The use of primer pair as defined by SEQ ID NOS# 1 and 3 in the system of claim 47 constitutes merely a procedural feature that is not an essential technical feature of the system but relates to a method of using the system rather than clearly defining the apparatus in terms of its technical features.
The intended limitations are therefore not clear from this claim, contrary to the requirements of Article 6 PCT.

Thus, claims 47-52 are unclear, contrary to the requirements of Article 6 PCT.

Possible steps after receipt of the international search report (ISR) and written opinion of the International Searching Authority (WO-ISA)

General information	For all international applications filed on or after 01/01/2004 the competent ISA will establish an ISR. It is accompanied by the WO-ISA. Unlike the former written opinion of the IPEA (Rule 66.2 PCT), the WO-ISA is not meant to be responded to, but to be taken into consideration for further procedural steps. This document explains about the possibilities.
Amending claims under Art. 19 PCT	Within 2 months after the date of mailing of the ISR and the WO-ISA the applicant may file amended claims under Art. 19 PCT directly with the International Bureau of WIPO. The PCT reform of 2004 did not change this procedure. For further information please see Rule 46 PCT as well as form PCT/ISA/220 and the corresponding Notes to form PCT/ISA/220.
Filing a demand for international preliminary examination	In principle, the WO-ISA will be considered as the written opinion of the IPEA. This should, in many cases, make it unnecessary to file a demand for international preliminary examination. If the applicant nevertheless wishes to file a demand this must be done before expiry of 3 months after the date of mailing of the ISR/WO-ISA or 22 months after priority date, whichever expires later (Rule 54bis PCT). Amendments under Art. 34 PCT can be filed with the IPEA as before, normally at the same time as filing the demand (Rule 66.1 (b) PCT). If a demand for international preliminary examination is filed and no comments/amendments have been received the WO-ISA will be transformed by the IPEA into an IPRP (International Preliminary Report on Patentability) which would merely reflect the content of the WO-ISA. The demand can still be withdrawn (Art. 37 PCT).
Filing informal comments	After receipt of the ISR/WO-ISA the applicant may file informal comments on the WO-ISA directly with the International Bureau of WIPO. These will be communicated to the designated Offices together with the IPRP (International Preliminary Report on Patentability) at 30 months from the priority date. Please also refer to the next box.
End of the international phase	At the end of the international phase the International Bureau of WIPO will transform the WO-ISA or, if a demand was filed, the written opinion of the IPEA into the IPRP, which will then be transmitted together with possible informal comments to the designated Offices. The IPRP replaces the former IPER (international preliminary examination report).
Relevant PCT Rules and more information	Rule 43 PCT, Rule 43bis PCT, Rule 44 PCT, Rule 44bis PCT, PCT Newsletter 12/2003, OJ 11/2003, OJ 12/2003